[CONTRIBUTION FROM THE DEPARTMENT OF PHARMACOLOGY, MEDICAL SCHOOL, STANFORD UNIVERSITY]

Substances Whose Optical Inactivity Can Be Attributed Only to Fourfold Alternating Axial Molecular Symmetry. III. A Second Example (*meso*-Pentaerythritol Tetramenthyloxyacetate)[1]

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The synthesis is reported of pentaerythritol di-(+)-menthyloxyacetate di-(−)-menthyloxyacetate, the second known example of a molecule which lacks any plane or center of symmetry but is superposable on its mirror image. Experimentally, the compound is optically inactive, as predicted. The inactivity is attributed to the presence of a fourfold alternating axis of molecular symmetry. The active (− − − −) diastereomer of this compound also was prepared.

In 1955, the preparation was reported[1a] of a substance (I) which was optically inactive although lacking any plane or center of molecular symmetry. This inactivity was attributed to the presence of a *fourfold alternating axis of symmetry*.[2,3] Any molecule containing this symmetry element (whether or not it contains other symmetry elements) is necessarily superposable on its mirror image.[4] The substance (I) presumably represented the first actual preparation[5] of any molecule of this unique symmetry type and, so far as we are aware, no additional examples have been reported since.

Since the behavior of a single example might not be regarded as rigorous proof for the general principle of optical inactivity mentioned above, we are now undertaking the preparation of a series of additional organic compounds, of diverse structural types, so chosen that in each case the molecule will possess a fourfold alternating axis as its only significant[6] symmetry element.

Aside from the spirane type,[7] *e.g.*, I, there have to our knowledge been only two explicit proposals of organic structural types which would exhibit alternating axial symmetry of the fourfold order *only*. One proposal was for molecules of a quaternary acyclic type,[8-11] illustrated by formula II, where the group A^+ is the non-superposable mirror image of A^-. This type would include derivatives of methane, neopentane or pentaerythritol,[12] each molecule containing a suitable set of four dissymmetric substituents.

The second proposal was for a quadrisymmetric cyclic type,[13] illustrated by certain 1,2,3,4-tetrasubstituted cyclobutanes of the all-*trans* configuration, *e.g.*, III. Certain 1,3,5,7-tetrasubstituted all-*trans*-cycloöctane derivatives[14] would also be appropriate. Because the symmetry relations of III are easily visualized and understood, this is perhaps the most frequently mentioned example of a molecule which would possess exclusively fourfold alternating axial symmetry.

One other possibility which we have considered would be a hindered biphenyl type, *e.g.*, IV. The *ortho* groups A^+ and A^- would be sufficiently bulky to maintain effective perpendicularity of the ring planes, in addition to meeting symmetry requirements.

It will be noted that compounds with fourfold alternating axial symmetry are usually to be sought among molecules with a *perpendobiplanar* structure, *i.e.*, a structure which may be regarded as consisting of two principal parts which are respectively situ-

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(1) For preceding (unnumbered) articles in this series, see (a) G. E. McCasland and S. Proskow, THIS JOURNAL, **77**, 4688 (1955); (b) **78**, 5646 (1956).

(2) The alternating symmetry axis has sometimes been termed a "mirror," "second order" or "composite" axis. Crystallographers prefer to employ a somewhat different concept, the "rotatory inversion" axis (see *Chemistry & Industry*, 1599 (1955)).

(3) (a) For discussions of symmetry theory as applied to organic chemistry, see the literature citations given in footnotes 5–10 of our previous article (ref. 1b); the discussion by G. W. Wheland (ref. 1b, footnote 9) is especially valuable. (b) For a briefer but more available discussion by F. M. Jaeger (ref. 1b, footnote 7), see the misleadingly titled book "Optical Activity and High Temperature Measurements," McGraw–Hill Book Co., Inc., New York, N. Y., 1930, Part I. (c) For more recent comment, see J. C. Speakman, "Progress in Stereochemistry," W. Klyne (Editor), Academic Press, Inc., New York, N. Y., 1958, Vol. II, p. 17.

(4) Image-superposability, although always a sufficient, is not always a necessary condition for optical inactivity of a substance (in the fluid state); see K. Mislow, *et al.*, *Science*, **120**, 232 (1954); THIS JOURNAL, **77**, 6712 (1955); *Trans. N. Y. Acad. Sci.*, **19**, 298 (1957).

(5) The *Chemical Abstracts* summary (**51**, 2731 (1957)) of our previous article erroneously states that salts of the spirane I are the ". . . 1st known substances to possess a fourfold alternating axis of symmetry." This statement should be corrected by appending the words ". . . *but no plane or center of symmetry*."

(6) The molecular symmetry elements significant as causes of optical inactivity are the onefold (plane), twofold (center), fourfold and 4 *n*-fold alternating axes; see ref. 1b, footnote 9.

(7) Numerous variations of the spirane type (formula I) are possible: The spiro nitrogen might be replaced by other tetrahedral atoms. The dissymmetric groups might be extensively varied. Ring size might be increased or decreased, the extreme case being an allene of type ($A^+A^+C{=}C{=}CA^-A^-$). Certain substituted linear polyspiranes (*e.g.*, with four rings) would have suitable symmetry.

(8) E. Mohr, *J. prakt. Chem.*, [2] **68**, 378 (1903). Although calling attention to the unusual stereoisomerism of the molecular type C $(CXYZ)_4$, Mohr did not explicitly mention pentaerythritol derivatives.

(9) F. Ebel in K. Freudenberg (Editor), "Stereochemie," F. Deuticke, Leipzig, 1933, p. 601.

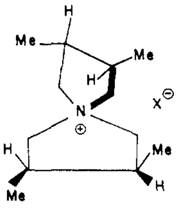
(10) R. L. Shriner and R. Adams in their well known discussion in Gilman's "Treatise" correctly predict one *meso* and two racemic forms for the molecular type $C(A^+A^+A^-A^-)$, but do not mention that the *meso* isomer would contain a (fourfold)) alternating axis of symmetry. See H. Gilman (Editor), "Organic Chemistry: An Advanced Treatise," 2nd ed., John Wiley and Sons, Inc., New York, N. Y., 1943, Vol. 1, p. 239.

(11) In the quaternary acyclic type the central carbon atom might be replaced by some other tetrahedral atom. The dissymmetric groups might contain cyclic structures.

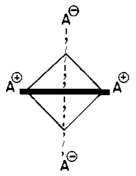
(12) For our early work on stereoisomerism of pentaerythritol derivatives, see the University of Toronto Ph.D. Theses of (a) D. A. Smith, 1951, and (b) S. Proskow, 1956; (c) see also G. E. McCasland and D. A. Smith, THIS JOURNAL, **74**, 564 (1952). (Correction: Change "three racemic forms" to "two racemic forms and one *meso* form.")

(13) In their 1943 discussion (ref. 10, p. 319) Shriner and Adams pointed out that cyclobutane derivatives such as III contain an "alternating axis of symmetry." However, it appears that their discussion did not offer any satisfactory definition for "alternating axis," and did not bring out the really unusual feature of the molecule III: the presence of a *fourfold* alternating axis in the absence of other significant symmetry elements.

(14) It is of interest that a cycloöctane derivative with eight suitable dissymmetric substituents in all-*trans* configuration would exhibit alternating axial symmetry of *eightfold order only*. No examples of this symmetry type have ever been prepared.



(I)



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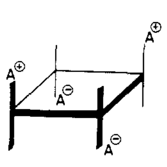

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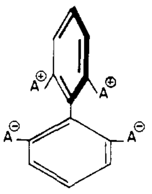

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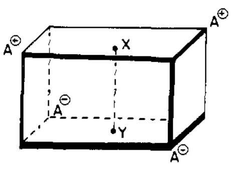
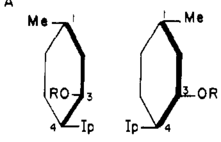
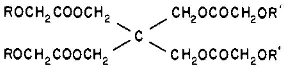


(V)



L(1,3)-(−) D(1,3)-(+)



$$\begin{matrix}\mathrm{ROCH_2COOCH_2} & & \mathrm{CH_2OCOCH_2OR'}\\ & \mathrm{C} & \\ \mathrm{ROCH_2COOCH_2} & & \mathrm{CH_2OCOCH_2OR'}\end{matrix}$$

VI, R = (+)-Menthyl , R' = (−)-Menthyl

VII, R = R' = (−)-Menthyl

(±)-VIII, R = H

(±)-IX, R = $-CH_2COOH$

(±)-X, R = $-CH_2COCl$

ated in two mutually perpendicular planes. Most of the stereoisomers here considered may also be classified as *dendroasymmetric*,[15] since they contain several dissymmetric groups attached directly or indirectly to the same central atom.

From more detailed consideration of the examples I, II, III and IV, one may induct a set of general rules for the construction of molecules meeting the prescribed symmetry conditions: (1) The molecule must contain four dissymmetric groups, $A^+A^+A^-A^-$, such that A^+ is the non-superposable mirror image of A^-; (2) these four groups must be situated at alternate lower and upper apices (formula V) of a right square prism[15a]; and (3) the mono- or polyatomic skeleton connecting the groups must itself possess a fourfold alternating axis coincident with the vertical axis (XY, formula V) of the prism.

It will be seen that lines connecting the four groups (formula V) will in general form a "semi-regular" tetrahedron. That is, the tetrahedron will have two edges of length a and four of length b ($a \neq b$); the two A^+ groups must then be on one of the a edges, the two A^- groups on the other. In the special case where the right square prism is a cube, the tetrahedron will be fully regular, and the two A^+ groups may then be on *any* two apices, leaving the two remaining apices for the A^- groups.

Since an example of the spirane type (formula I) had already been studied, our present choice of a model compound for synthesis was made from the types illustrated by formulas II, III and IV. Type III although simple in conception would be expected to present formidable synthetic obstacles, partly because of the large number of possible diastereomers (there would be four even if the ring were limited to its all-*trans* configuration). Type IV, with not more than four possible diastereomers, might be somewhat easier to prepare. Type II was clearly the most attractive choice, since the final product can exist in only three diastereomeric forms, since the preparative reactions are straightforward, and since the cheap and available pentaerythritol furnishes a convenient starting point for synthesis.

The suitability of pentaerythritol as a starting material for preparing stereoisomers of unusual nature was recognized as long ago as 1933 by F. Ebel.[9] For example, if one is able to esterify *any* two of the four pentaerythritol hydroxyls with *any* dextrorotatory acid, subsequent esterification of the remaining hydroxyls with the corresponding levorotatory acid will immediately produce a tetraester with the desired symmetry characteristics. Instead of a tetraester, one might equally well elect to prepare a tetraether, tetraurethan, etc., provided that in each case a suitable pair of pure enantiomeric reagents is available. Our own experiments on the preparation of these various types of pentaerythritol derivatives began[12] in 1950, and have now been successfully completed with the synthesis of pentaerythritol di-(+)-menthyloxyacetate di-(−)-menthyloxyacetate (VI).

On grounds of logical simplicity it might seem preferable to prepare the desired pentaerythritol tetraester from some optically active acid (*e.g.*, lactic acid) with but a single asymmetric carbon atom. For reasons of practical synthetic convenience, however, we have in our present work employed the more complex menthyloxyacetic acid, (±)-IX, with three asymmetric carbon atoms. The number of asymmetric carbon atoms in each A^+ or A^- group does not matter as long as the groups are dissymmetric and have the relationship of non-superposable mirror images.

For pentaerythritol tetramenthyloxyacetate three diastereomers would be predicted,[9,10] one *meso* and two active. The inactive, *meso* diastereomer, symbolized by (++−−), is superposable on its mirror image. The active diastereomers (++++) and (+++−) are predicted to have corresponding enantiomeric forms (−−−−) and (−−−+) of opposite rotations. The symbols refer to the rotations (not configurations[16]) of the corresponding four molecules of free menthyloxyacetic acid which would result on hydrolysis. In addition to the *meso* diastereomer we have prepared the active (−−−−) diastereomer VII. It appears

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[15] *Dendroasymmetric:* a term proposed by C. R. Noller, Chemistry Department, Stanford University. Recent interest in this class of stereoisomers is largely due to the well known and independent work of Professor Noller. Our own interest in dendroasymmetric molecules is limited to those rather exceptional examples which exhibit fourfold alternating axial symmetry.

[15a] Footnote added in proof.—It has been pointed out that the drawing V might be misinterpreted. In reality the top and bottom faces of the prism shown should be visualized as square; the remaining four faces might be either square or rectangular.

[16] Since no rational system for designating terpene stereoisomers has been adopted, meaningless and arbitrary prefixes (*e.g.*, "neo," "isoneo") are commonly employed. Formulas VIII–X illustrate the possibility of designating monocyclic terpene configurations by systematic numerical prefixes. For example, the prefix "L(1,3)-" for ordinary levorotatory menthol signifies that the (methyl and hydroxy) groups at positions 1 and 3 are to the *left* of the properly oriented perspective formula, (−)-VIII; the (isopropyl) group at 4 is then assumed to be on the right. For further explanation, see the pamphlet, "A New General System for the Naming of Stereoisomers," available from the Chemical Abstracts Service, c/o Ohio State University, Columbus 10, Ohio. (*Note:* The *Chemical Abstracts* ring-numbering for menthols here used deviates from that used by *C. A.* for other alkylated cyclohexanols.)

that preparation of the active diastereomer $(+++-)$ or $(---+)$ might be considerably more difficult.

It has been established recently that the common levorotatory stereoisomer of menthol (4-isopropyl-1-methyl-3-cyclohexanol) has the absolute L(1,3)-configuration,[16] (−)-VIII. It happens that the menthyloxyacetic acid and acid chloride of corresponding configuration are also levorotatory. This information serves to establish the absolute configurations of all the menthyloxyacetyl derivatives herein reported.

Much credit should be given to E. Mohr who (with O. Aschan) first recognized[8] the unusual symmetry characteristics of the molecular type $C(CXYZ)_4$. However, Mohr did make one statement[8] which now appears to have been incorrect. When testing image-superposability of any molecule, it is customary to assume, first that some symmetric conformation (if any exists) will be selected for examination and, second, that both object and image conformations must remain rigidly fixed during the superposition process. Thus superposition can be attempted only by moving or rotating the object molecule *as a whole.*

Mohr, however, claimed that for a molecule of the type $C(CXYZ)_4$ (*meso* diastereomer) there does not exist *any* conformation which can be superposed on its image, unless one breaks the above rule by changing the object molecule conformation after fixing its image. With molecular models one can demonstrate easily that this conclusion of Mohr was erroneous: all that is necessary is to observe the standard rule that a *symmetric* conformation should be chosen for examination. In this case, the symmetric conformations will be those which possess fourfold alternating axes. The question here involved is of some importance, since Mislow[4] recently has reported a genuine example of an object molecule (of an inactive, non-racemic substance) *no* conformation of which can be directly superposed on its image.

In order to prepare the *meso* tetraester VI, two of the four pentaerythritol hydroxyls were protected by acetonation.[17] After acylation with (−)-menthyloxyacetyl chloride,[18] the isopropylidene group was removed by mild acid hydrolysis, and the liberated hydroxyls then esterified with the (+)-acid chloride.[19] The conditions for successful deacetonation are critical, and quantitative control for this step was found essential. The disappearance, reappearance and final disappearance of hydroxy groups was nicely confirmed by changes in the infrared spectra. The intermediates and final product were unexpectedly difficult to crystallize, and chromatographic purifications were found essential. The active $(----)$ diastereomer was readily obtained by direct acylation of pentaerythritol itself with four moles of the appropriate acid chloride.

As Djerassi[20] has pointed out, the traditional choice of the sodium D line for polarimetric observation has been rather unfortunate, since many compounds which appear almost inactive at this wave length would display specific rotations of hundreds or even thousands of degrees at shorter wave lengths, especially in the near ultraviolet. In order to make a more rigorous test for possible activity in our tetraester VI we examined it over an extended range of wave lengths, from 680 to 380 mμ. Even under these drastic conditions, the maximum observed deviation from zero rotation did not exceed 0.06°. Thus the compound may be regarded as having zero rotation within experimental error, in accord with prediction.

The melting point (65°) for the final *meso* tetraester is surprisingly low for a molecule of such high symmetry and high molecular weight. A possible explanation is that the 53 carbon atoms surround the oxygen atoms in such a manner as to give the compound hydrocarbon-like properties.

Samples of the compounds herein described are being submitted to Professor Arthur Furst of the Stanford Medical School for biological tests as potential anticancer agents.

Acknowledgment.—We would like to thank Professor J. B. Neilands and Mr. Don Sproul, Biochemistry Department, University of California, Berkeley, for use of the spectropolarimeter designed by them. We are indebted to Professor Arthur Furst, Stanford Medical School, for helpful advice and use of facilities. Generous financial support was provided by an Institutional Grant from the American Cancer Society.

Experimental

All melting and boiling points have been corrected. Melting points were determined with a Monoscop micro hot-stage. Microanalyses were made by the Micro-Tech Laboratories, Skokie, Ill. Infrared spectra were determined with a Perkin-Elmer model 21 recording infrared spectrometer, using potassium bromide pellets. Optical rotations at 589 mμ (sodium D line) were determined with a modified Winkel-Zeiss double field polarimeter, and at other wave lengths with a photoelectric spectropolarimeter (see below).

***O,O*-Isopropylidenepentaerythritol Di-(−)-menthyloxyacetate.**—To a solution of 1.0 g. of *O,O*-isopropylidenepentaerythritol[17] (m.p. 128–129°) in 30 ml. of anhydrous pyridine at 0° there was added gradually 3.0 g. of colorless, liquid (−)-menthyloxyacetyl chloride[18] (b.p. 114–116° (1–3 mm.), $[\alpha]^{25}\text{D}$ −89.2°). The solution was kept at 25° for 12 hours. After addition of 60 ml. of water, the mixture was extracted with three 50-ml. portions of ether. The combined ether extracts were washed successively with *M* hydrochloric acid, saturated sodium bicarbonate, and water. After drying the solution with anhydrous sodium sulfate, the ether was removed by vacuum distillation, giving a colorless crystalline residue weighing 1.17 g. (36%), m.p. 81–82°.

A 52-mg. portion of this material in 35 ml. of petroleum ether (b.p. 35–55°) was passed over a 1.2 × 3.5 cm. column

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(17) For literature references on the acetonation of pentaerythritol, see (a) E. Berlow, *et al.*, "The Pentaerythritols," Reinhold Publ. Corp., New York, N. Y., 1958, Chap. 11, p. 166; (b) S. F. Marrian, *Chem. Revs.*, **43**, 149 (1948).

(18) The Leffler–Calkin procedure for (−)-menthyloxyacetic acid ("Organic Syntheses," Coll. Vol. III, pp. 547–1955) was modified by using *equimolar* quantities of menthol, *lithium* (instead of sodium) metal, and (finely powdered, anhydrous) *sodium* chloroacetate. The yield based on menthol is thus raised from 33 to 83%, and recycling becomes unnecessary. The acid was converted to its chloride in the usual manner.

(19) (a) C. R. Noller of the Department of Chemistry of Stanford University, in an application for a grant from the National Science Foundation, made in November, 1957, proposed a similar series of reactions for the synthesis of compounds of the type CA(+)A(−)B(+)R and CA(+)A(−)B(+)B(−) and expects to pursue this work at the first opportunity. (b) Commercial racemic menthol (tested and purified to exclude contaminating diastereomers often present) was resolved by the method of A. W. Ingersoll ("Organic Reactions," Vol. II, 1944, pp. 381–382, 398–400). (+)-Menthyloxyacetic acid was prepared by the above lithium procedure, and converted to its chloride in the usual manner.

(20) See *Chem. Eng. News*, **35**, 40 (1957).

of activity grade III[21a,b] aluminum oxide (prewet with petroleum ether). After development with 35 ml. of petroleum ether, the column was successively eluted with 35 ml. additional petroleum ether and with 35 ml. of 1:1 benzene-petroleum ether. Evaporation of the combined eluates gave a residue of 35 mg. of colorless needles, m.p. unchanged, $[\alpha]_D^{25}$ −72.0° (chloroform, *c* 1). For analysis, a sample of the chromatographed product was recrystallized from a small volume of *n*-pentane by prolonged cooling to −10°.

Anal. Calcd. for $C_{32}H_{56}O_8$: C, 67.57; H, 9.93. Found: C, 67.74; H, 9.76.

The infrared spectrum showed strong C=O and C—O stretching vibrations at 1760 and 1130 cm.$^{-1}$, respectively. A comparison spectrum on the isopropylidenepentaerythritol starting material lacked this C=O stretching absorption, and showed strong O—H stretching and bending vibrations at 3250 and 1380 cm.$^{-1}$ not shown by the acetonated diester. The starting material also showed C—O stretching vibrations at 1040, 1150 and 1200 cm.$^{-1}$.

Pentaerythritol Di-(−)-menthyloxyacetate.—A 120-mg. portion of recrystallized commercial 2,4-dinitrophenylhydrazine was dissolved in 46 ml. of 5.5 *M* hydrochloric acid, and the resulting solution diluted with water to 125 ml.

The acetonated diester (1.5 g., not chromatographed) was dissolved in 40 ml. of 3:1 dioxane-water. After addition of 0.5 ml. of 12 *M* hydrochloric acid, the mixture was heated to 80–90° (100° bath), while a current of nitrogen gas was passed through it. The vapor stream was passed under the surface of the dinitrophenylhydrazine solution, causing a precipitate to form. After 10 minutes, a second 0.5-ml. portion of hydrochloric acid was added, and the distillation continued (for about 10 minutes) until no further precipitate was obtained.

The cooled liquid distillation residue was neutralized with powdered sodium bicarbonate, and the resulting solution vacuum distilled to dryness. The partly crystalline residue was extracted with 150 ml. of chloroform, and the extract filtered. On vacuum distillation a residue of 1.3 g. of colorless oily product was obtained.

A solution of this product in 10 ml. of petroleum ether (b.p. 35–50°) was passed over a 50-g. column of Florisil[21c] (prewet with petroleum ether). The column was developed with 200 ml. of petroleum ether and with 200 ml. of 4:1 petroleum ether–chloroform. It was then eluted with 500 ml. of chloroform. By evaporation of the eluate there was obtained 636 mg. (43%) of the diester, an oil which changed on standing into colorless needles. For analysis, a sample was recrystallized from a small volume of *n*-pentane, by prolonged cooling to −10°, giving colorless needles, m.p. 63–64°, $[\alpha]^{25}D$ −74.4° (chloroform, *c* 1). The infrared spectrum, unlike that of the starting material, showed strong O–H stretching and bending vibrations at 3250 and 1280 cm.$^{-1}$, respectively. It also showed C=O stretching vibrations at 1740 cm.$^{-1}$ and C—O stretching vibrations at 1190, 1120 and 1050 cm.$^{-1}$.

Anal. Calcd. for $C_{29}H_{52}O_8$: C, 65.88; H, 9.91. Found: C, 66.01; H, 9.88.

Pentaerythritol Di-(+)-menthyloxyacetate Di-(−)-methyloxyacetate (*meso* Diastereomer).—To a solution of 320 mg. of the di-(−)-ester in 10.0 ml. of anhydrous pyridine at 0° was added 280 mg. of (+)-menthyloxyacetyl chloride[19] (b.p. 109–110° (2 mm.)). The mixture was kept overnight at 25° and then diluted with 30 ml. of water. The resulting mixture was extracted with three 50-ml. portions of ether.

The combined ether extracts were successively washed with *M* hydrochloric acid, saturated sodium bicarbonate, and water. The ethereal solution was dried with anhydrous sodium sulfate, and vacuum distilled to dryness, giving 572 mg. of colorless, viscous liquid residue.

A solution of this material in 2 ml. of petroleum ether (b.p. 35–50°) was passed over a 1.5 × 15 cm. column of activity grade III[21a,b] aluminum oxide (prewet with petroleum ether). After development with 30 ml. of petroleum ether, the column was successively eluted with 120 ml. of petroleum ether and with 60 ml. of 4:1 petroleum ether–benzene. The combined eluates were vacuum distilled to dryness, giving 431 mg. of colorless oily product.

The product was dissolved in a minimum volume of boiling methanol. After prolonged standing (two weeks) of the solution at −10°, the product separated in the form of colorless prisms, weight about 300 mg. (58%), m.p. 64–65°.

A sample was recrystallized several times more from methanol, for analysis, giving colorless prisms, m.p. 68.5–70.0°, $[\alpha]^{25}D$ 0.00° (chloroform, *c* 10). The infrared spectrum was lacking in O–H stretching and bending vibrations, but did show strong C=O and C—O stretching vibrations at 1755 and at 1180 and 1120 cm.$^{-1}$, respectively.

Anal. Calcd. for $C_{53}H_{92}O_{12}$: C, 69.10; H, 10.07. Found: C, 69.10; H, 9.96.

The optical rotation of the *meso* tetraester also was examined over an extended wave length range, from 680 to 380 mμ, using a recording photoelectric spectropolarimeter. This instrument (constructed by Mr. Donald Sproul—see Acknowledgment) consisted of a modified Rudolph no. 202 photoelectric polarimeter, provided with an oscillating polarizer and coupled to a Beckman monochromator with tungsten lamp or xenon arc light source and automatic wave length drive. The analyzer was connected through a photomultiplier tube and amplifier to a Brown (Minneapolis–Honeywell) recorder.

The sample, examined in a one decimeter tube with quartz end plates (chloroform, *c* 4) at 25° showed a very slight levorotation (presumably due to traces of impurities) which varied from 0.00 to −0.06° (after correction for solvent blank) over the wave length range 680 to 380 mμ. The rotation of the *meso* tetraester may thus be regarded as zero within experimental error.

Pentaerythritol Tetra-(−)-menthyloxyacetate: Active (− − − −) Diastereomer.—A 68-mg. sample of dry, finely powdered pentaerythritol was treated with 4.0 equivalents of (−)-menthyloxyacetyl chloride in anhydrous pyridine, by essentially the procedure described above for the *meso* tetraester. A small yield of the (− − − −) diastereomer was obtained in the form of colorless blades, m.p. 65–66°, $[\alpha]^{29}D$ −90.7° (chloroform, *c* 1).

Anal. Calcd. for $C_{53}H_{92}O_{12}$: C, 69.10; H, 10.07. Found: C, 69.05; H, 10.05.

Stanford, Calif.

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[21] (a) P. B. Mueller, *Helv. Chim. Acta*, **26**, 1945 (1943); (b) H. Brockman and H. Schodder, *Ber.*, **74**, 73 (1941); (c) A special preparation of aluminum silicate (Fullers' earth) from the Floridin Co., Tallahassee, Fla.